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Applicants: GARTH J.S. COOPER)
Serial No. 715,031)
Filed: June 10, 1991)
For: TREATMENT OF DIABETES)
MELLITUS)

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LEE, LASTER

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TRANSMITTAL LETTER

Honorable Commissioner of
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Bradford J. Duft, Esq.
Registration No. 32,219
Bradford J. Duft
Signature
7-23-91
Date of Signature

Dear Sir:

Transmitted herewith for filing in the above-identified application are the following documents:

- 1) Declaration under 37 C.F.R. § 1.132.
- 2) Amendment.
- 3) A return postpaid card acknowledging receipt of above-identified material.

The Commissioner is hereby authorized to charge any fees associated with the present filing to Deposit Account No. 12-2475.

Respectfully submitted,
LYON & LYON

Date: 7-23-91

By: *Bradford J. Duft*
Bradford J. Duft, Esq.
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1986-1989: neurophysiological studies into the mechanisms of "thermanalgesia", the control of pain by topically applied heat.
1989-91: studies into the role of amylin hormone in normal and abnormal carbohydrate metabolism. Studies of effects of amylin on skeletal muscle and the whole animal, and its possible role in the pathogenesis of peripheral insulin resistance and type-2 diabetes. Studies of the role of amylin deficiency complicating the therapy of type-1 diabetes.

Clinical Experience:

1978: Junior Medical Officer, Auckland Hospital Board
1979: Senior Medical Officer, Auckland Hospital Board
1979-1984: Physician, Weekend Medical Services, Howick, New Zealand.
1984-1987: Clinical Research Scientist as described above.
1987-1989: Physician, Union Health Centre, Otahuhu, Auckland.

PROFESSIONAL ACTIVITIES/SOCIETIES:

Council Member, New Zealand Physiological Society
Member, Australian Physiological and Pharmacological Society
Member, Australian Neuroscience Society
1975-1983: Medical Officer (Capt), 1st Field Hospital, Territorial Force, New Zealand Army
Member, American Diabetes Association

INVITED LECTURES

Plenary Lecture, joint meeting of Physiological Society/Endocrine Society/Society for the Study of Diabetes, Wellington, New Zealand, May 1987

Invited Speaker, Regional Thermoregulatory Group, Prague, Czechoslovakia, July 1989

PUBLICATIONS:

Papers:

Young, A.A. and Dawson, N.J. (1982) Evidence for on/off control of heat-dissipation from the tail of the rat **Canadian Journal of Physiology and Pharmacology** 60:392-398

Dawson, N.J. Hellon, R.F. Herington, J.G. and Young, A.A. (1982) Facial thermal input in the caudal trigeminal nucleus of rats reared at 30°C **Journal of Physiology** 333:545-554

Young, A.A. (1978) Clothing man in a cold environment. Inaugural edition **New Zealand Antarctic Record**

Young, A.A. and Dawson, N.J. (1984) The dynamic properties of trigeminal thermoreceptors following heat-rearing in rats **Pflügers Archiv** 401:213-215.

Bogardus, C., Lillioja, S., Mott, D., Zawadski, J., Young, A., and Abbott, W. (1985) Evidence for reduced thermic effect of insulin and glucose infusions in Pima Indians **Journal of Clinical Investigation** 75:1264-1269

DeFreitas, C.R., Dawson, N.J., Young, A.A. and Mackey, W.J. (1985) Microclimate and heat-stress of runners in mass participation events **Journal of Climate and Applied Meteorology** 24:184-191

Lillioja, S., Mott, D.M., Zawadski, J.K., Young, A.A., Abbott, W.G. and Bogardus, C. (1986) Glucose storage is a major determinant of in vivo "insulin resistance" in subjects with normal glucose tolerance **Journal of Clinical Endocrinology and Metabolism** 62(5):922-927

Bogardus, C., Lillioja, S., Ravussin, E., Abbott, W., Zawadzki, J., Young, A., Knowler, W., Jacobowitz, R. and Moll, P. (1986) Familial dependence of the resting metabolic rate **New England Journal of Medicine** 315:96-100

Dawson, N.J., Houseley, G.D. and Young, A.A. (1986) Rearing rats (*Rattus norvegicus*) at 30°C does not alter sensitivity to noradrenaline **Comparative Biochemistry and Physiology [A]** 85(1):191-195

Young, A.A., Mott, D.M., Stone, K. and Bogardus, C. (1988) Insulin response of components of whole-body and muscle carbohydrate metabolism in humans **American Journal of Physiology** 254(2 Pt 1): E231-236

Young, A.A. (1987) Thermal sensations during simultaneous warming and cooling at the forearm: a human psychophysical study **Journal of Thermal Biology** 12(4):243-247

Young, A.A. and Dawson, N.J. (1987) Static and dynamic response characteristics, receptive fields and interaction with noxious input of medullary thermoresponsive neurones in the rat **Journal of Neurophysiology** 57:1925-1936

Lillioja, S., D.M.Mott, J.K.Zawadski, A.A.Young, W.G.Abbott, W.C.Knowler, P.H.Bennett, P.Moll and C.Bogardus (1987) In vivo insulin action is a familial characteristic in non-diabetic Pima Indians **Diabetes** 36(11): 1329-1335

Young, A.A. and N.J.Dawson (1987) Effects of environmental temperature on the development of a noradrenergic thermoregulatory mechanism in the rat. **Pflügers Archiv** 412(1-2):141-146

Abbott, W.G.H., S.Lillioja, A.A.Young, J.K.Zawadski, H.Yki-Järvinen, L.Christin and B.V.Howard (1987) Relationships between plasma lipoprotein concentrations and insulin action in an obese hyperinsulinemic population **Diabetes** 36:897-904

Lillioja, S., Young, A.A., C.L.Cutler, J.L.Ivy, W.G.H.Abbott, J.K.Zawadski, H.Yki-Järvinen, L.Christin, T.W.Secomb and C.Bogardus (1987) Skeletal muscle capillary density and fiber type are possible determinants of in vivo insulin resistance in man **Journal of Clinical Investigation** 80:415-424

Yki-Järvinen, H., Young, A.A., Lamkin, C. and Foley, J.E. (1987) Kinetics of glucose disposal in whole body and across skeletal muscle in man **Journal of Clinical Investigation** 79:1713-1719

Young, A.A., Mott, D.M., Wolfe-Lopez, D. and Bogardus, C. (1988) Muscle glycogen synthesis and disposition of infused glucose in human subjects with reduced rates of insulin-mediated carbohydrate storage **Diabetes** 37(3):303-308

Yki-Järvinen, H., Mott, D.M., Young, A.A., Stone, K. and Bogardus, C. (1987) Regulation of glycogen synthase and phosphorylase activities by glucose and insulin in human skeletal muscle *Journal of Clinical Investigation* 80:95-100

Yki-Järvinen, H., Consoli, A., Nurjahan, N., Young, A.A. and Gerich, J.E. (1987) Mechanism for underestimation of isotopically determined glucose disposal *Diabetes* 38(6):744-751

Yki-Järvinen, H., Kubo, K., Zawadski, J., Lillioja, S., Young, A., Abbot, W. and Foley, J.E. (1987) Dissociation of in vitro sensitivities of glucose transport and antilipolysis to insulin in NIDDM *American Journal of Physiology (Endocrinology and Metabolism)* 253:E300-E304

Young, A.A., Wang, M.-W. and Cooper, G.J.S. (1990) Amylin induces hyperglycemia, elevated blood lactate and increased glucose production *in vivo*: a proposed mechanism for hormonal control of the Cori cycle (submitted)

Wang, M.-W., Cooper, G.J.S. and Young, A.A. (1990) Dose-response characteristics for effects of amylin on plasma glucose, lactate, calcium, blood pressure and endogenous glucose production in the rat (in preparation)

Young, A.A., Wang, M.-W. and Cooper, G.J.S. (1991) A comparison of the actions of amylin and glucagon: implications for rescue from hypoglycemia (in preparation)

Young, A.A., Mott, D.M., Stone, K. and Cooper, G.J.S. (1991) Amylin activates glycogen phosphorylase in the isolated soleus muscle of the rat *FEBS Letters* 281(1/2): 149-151

Young, A.A., Gedulin, B., Lopez, D., Greene, H. and Cooper, G.J.S. (1991) Interaction of amylin and insulin in the isolated soleus muscle of the rat (submitted)

Gedulin, B., Cooper, G.J.S. and Young, A.A. (1991) Insulin and amylin secretion from isolated perfused pancreas from normal and diabetic fatty Zucker rats. (in preparation)

Albrecht, E., Young, A.A., Cooper, G.J.S. and Lehman-deGaeta, L.S. Synthesis and biological activity of human and canine amylin. *International Journal of Protein and Peptide Research* (submitted), 1991.

Monograph Entries:

Dawson, N.J. Young, A.A. and Dale Ormrod, D.G.C. (1984) Is there a critical period during which environment modifies the developing thermoregulatory system In: *Thermal Physiology*, Ed. Hales, J.R.S., Raven, New York, pp109-112

Young, A.A. Dawson, N.J. Hellon, R.F. and Herington, J.G. (1984) Static and dynamic properties of cells subserving facial thermoreception in heat-reared rats. In: **Thermal Physiology**, Ed. Hales, J.R.S., Raven, New York, pp13-16

Dawson, N.J., de Freitas, C.R., Mackey, W.J. and Young, A.A. (1987) The stressful climate created by massed fun-runners. In: **Heat Stress, Physical Exertion and Environment**, Eds Hales, J.R.S. and Richards, D.A.B., Elsevier, Amsterdam, pp77-82

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Reports and Theses:

Young, A.A. (1977) The rat tail, its importance in the regulation of body temperature. M.Sc. Thesis, University of Auckland.

Young, A.A. (1979) A comparison of the properties of down and polyester filled clothing in Antarctic use. Report to the Department of Scientific and Industrial Research, Antarctic Division.

Young, A.A. (1979) Report to the Commission of Inquiry into Freezer Temperatures: physiological aspects of working in freezers. Report commissioned by the New Zealand Freezing Companies Association.

Young, A.A. (1985) Thermoreception, thermoregulation and the early thermal environment. Ph.D. Thesis, University of Auckland.

Abstracts, Proceedings and Short Communications:

Young, A.A. and Dawson, N.J. (1981) On/off control of thermoregulatory vasodilation at the tail of the rat. *Proceedings of the Australian Physiological and Pharmacological Society*, 12(2):211P.

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Cook, C.J., Dawson, N.J. and Young, A.A. (1983) Does neonatal heat exposure affect processing at nucleus raphe magnus? **Proceedings of the International Union of Physiological Sciences 15:495 (29th IUPS, Sydney)**

Dawson, N.J. Housley, G.D. and Young, A.A. (1984) Sensitivity to noradrenaline is similar in rats reared at 20°C and 30°C. **Proceedings of the Physiological Society of New Zealand 4:61.**

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Young, A.A. and Mott, D. (1985) Insulin-sensitivity of simultaneously measured glucose disposal, carbohydrate storage and muscle glycogen synthase activity in man. **Clinical Research, 33(2):447A (National Meeting, American Federation of Clinical Research, Washington)**

Lillioja, S. Mott, D. Zawadski, J. Abbott, W.G. Young, A.A. and Bogardus, C. (1984) In vivo insulin resistance is associated with low glucose storage rates. **Abstract:**

Young, A.A. Stone, K. and Mott, D. (1984) Fluorimetric analysis of glycogenic substrates in milligram samples of human muscle. **Federation Proceedings 44(5):5642 (Federated American Societies for Experimental Biology, Anaheim)**

Bogardus, C. Lillioja, S. Zawadski, J. Young, A. and Abbott, W. (1984) Decreased thermic effect of insulin in Pima Indians. **Abstract: North American Association for Study of Obesity**

Young, A.A. Bogardus, C. and Mott, D. (1985) The contribution of carbohydrate storage to glucose disposal as a function of insulin concentration. **Diabetes 34:23A (American Diabetes Association, Baltimore, June 1985)**

Lillioja, S. J. Zawadski, A. Young, W. Abbott and C. Bogardus (1986) Acute insulin response and in vivo insulin action are independently correlated with glucose tolerance in Pima Indians. *Clinical Research*, 34(1): 61A. (Western Section, American Federation for Clinical Research)

Young, A. C. Bogardus and D. Mott (1986) Evidence from muscle glucose-6-phosphate levels that insulin resistance in man has a post-transport component. *Clinical Research*, 34(1): 67A. (Western Section, American Federation for Clinical Research)

Mott, D. C. Bogardus and A. Young (1986) Evidence in human muscle for a parallel mechanism regulating total glycogen phosphorylase and total glycogen synthase. *Clinical Research*, 34(1): 62A. (Western Section, American Federation for Clinical Research)

Bogardus, C. S. Lillioja, W. Abbott, J. Zawadski, A. Young and W. Knowler (1986) Resting metabolic rate is a familial trait. *Clinical Research*, 34(1): 71A. (Western Section, American Federation for Clinical Research)

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Bogardus, C., S. Lillioja, J. Zawadzki, A. Young, W. Abbott, G. Reaven, W. Knowler, P. Bennett, D. Mott, B. Howard and J. Foley (1986) Prospective study of metabolic changes during transition from normal to impaired glucose tolerance. *Clinical Research*, 34(2): 681A. (National Meeting, American Federation for Clinical Research)

Young, A. A., N. J. Dawson and J. P. Quinn (1986) Independent clamps of core and skin temperature during studies of central thermoresponsive neurones in the rat. Abstract: Thermal Physiology Satellite Symposium of the XXX International Congress of Physiological Sciences (Calgary, July 1986)

Young, A. A. (1986) Fused thermal sensation at the forearm during simultaneous heating and cooling using an "interposed-grid" configuration. Abstract: Thermal Physiology Satellite Symposium of the XXX International Congress of Physiological Sciences (Calgary, July 1986)

Yki-Jarvinen, H., A. A. Young, C. Bogardus and J. E. Foley (1986) Effect of hyperglycemia on glucose disposal in whole body and skeletal muscle in man. Abstract: European Association for the Study of Diabetes (Rome, September 1986)

Young,A.A. and D.M.Mott (1986) Coincidence of insulin-mediated changes in muscle glucose-6-phosphate, carbohydrate storage and glycogen synthase activity. *Diabetes*, 35: suppl 1, 84A. (Annual Meeting, American Diabetes Association, Anaheim, June 1986)

Bogardus,C., S.Lillioja, J.L.Ivy, C.Cutler, A.Young and W.Abbott (1986) Reduced capillary density in skeletal muscle associated with obesity is a mechanism for in vivo insulin resistance. *Diabetes*, 35: suppl 1, 14A. (Annual Meeting, American Diabetes Association, Anaheim, June 1986)

Abbott,W.G.H., S.Lillioja, A.Young, J.Zawadski, L.Christin, H.Yki-Jarvinen and B.V.Howard (1986) Lipoproteins and Insulin Resistance. (59th Meeting, American Heart Association, Dallas, 1986)

Young,A.A. (1987) Muscle glycogen synthesis and glucose "storage" in man *Proceedings of the Physiological Society of New Zealand* 7:69 (abstract: Control Systems in Health and Disease, Auckland, 1987)

Young,A.A., Moravec,J. and Pierau, Fr.-K. (1987) Temperature response characteristics of neurones in the lumbar dorsal horn of the rat *Proceedings of the Physiological Society of New Zealand* 7:4

Yki-Järvinen,H., Young,A. and Foley,J.E. (1987) Insulin-stimulated glucose disposal does not follow Michaelis-Menten kinetics with a K_m characteristic of the glucose transport system in whole body or in skeletal muscle in man *Clinical Research* 35(3):520A (abstract: American Federation for Clinical Research)

Young,A.A. (1988) Determinants of glucose disposal in man in health and in "insulin-resistance" *Proceedings of the Physiological Society of New Zealand* 8:14

Young,A.A. (1989) Responses of cold-responsive neurones at the caudal trigeminal nucleus of the rat to centre/surround thermal stimulation at the face *Proceedings of the Physiological Society of New Zealand* 9:51

Jones,G.A.C. and Young,A.A. (1989) Spinal cord responses to knee joint stimulation in the rat *Proceedings of the Physiological Society of New Zealand* 9:55

Wang,M.-W., Cooper,G.J.S. and Young,A.A. (1990) Dose response characteristics for the hyperglycemic, hyperlactemic, hypotensive and hypocalcemic effects of amylin in the rat *Proceedings: 14th International Diabetes Federation Congress, June 1991, Washington D.C.*

Rink, T.J., Young, A.A., Wang, M.-W., Gedulin, B.R., Mott, D.M. and Cooper, G.J.S. (1990) Amylin hormone has complementary actions to insulin in control of Cori cycle activity **Proceedings: 14th International Diabetes Federation Congress, June 1991, Washington D.C.**

Young, A.A., Wang, M.-W., Cooper, G.J.S. and Mott, D.M. (1990) Amylin and insulin exert complementary control over Cori cycle activity **Journal of Cellular Biochemistry Suppl. 15B: 68**

Young, A.A., Wang, M.-W., Cooper, G.J.S. (1990) Amylin, but not glucagon, acts to produce hyperglycemia, and elevated blood lactate and hepatic glucose production in the fasted rat **Proceedings: 14th International Diabetes Federation Congress, June 1991, Washington D.C.**

Huang, H.-J.S., Cooper, G.J.S., Young, A.A. and Johnson, M.J. (1990) Deficiency of amylin expression in the pancreas of auto-immune BB/Wor diabetic rats **Journal of Cellular Biochemistry Suppl. 15B: 67**

Cooper, G.J.S., Young, A.A., Gedulin, B.R., Johnson, M.J. and Huang, H.-J.S. (1991) Elevation of amylin gene-expression is consistent with a role for this hormone in the causation of insulin resistance in the rat. **Journal of Cellular Biochemistry Suppl. 15B: 65.**

Young, A. A., M.-W. Wang, T. J. Rink, and G. J. S. Cooper. Effects of intravenous injections of amylin in the fasted, anaesthetized rat. **Journal of Physiology (Proceedings)** (in press), 1991.